Cannabis compound slows lung cancer in mice

The active compound in marijuana, THC, can slow the growth of lung tumours and reduce the spread of the cancer in mice, a preliminary study reveals.

Human lung cancer tumours grew less than half as fast in mice that received moderate doses of the compound, the researchers reveal. They hope that drugs mimicking the apparent anti-cancer effects of tetrahydrocanabinol (THC) could one day help treat patients. The team strongly discourage people from self-medicating by smoking marijuana, noting that doing so could potentially encourage tumour growth.

Ramesh Ganju at the Harvard Cancer Center in Boston, Massachusetts, US, and colleagues deposited human lung cancer cells under the skin of a dozen mice and allowed the tumours to grow in the animals for about two weeks. They then began giving half of these mice daily injections of about 250 micrograms of synthetic THC right next to the tumours for three weeks. A cannabis cigarette may contain as much as 150 milligrams of THC.

Tumours in the control mice averaged about 0.6 grams in weight by the end of the five-week trial. By comparison, those in the mice that received THC weighed just 0.25 grams – 60% less.

Blood blocker

In a separate experiment to test whether THC could slow the spread of cancer cells (metastasis), the researchers injected human lung cancer cells into the tail veins of mice to mimic such a spread. The team immediately started giving half of these animals a daily 250 microgram injection of THC for three weeks. They found 60% fewer cancerous lesions in the mice that received THC compared to the control animals.

Ganju believes that THC inhibits cancer growth by blocking the formation of blood vessels within tumours. Previous tests on human lung cancer cells in a dish suggested that THC blocked the signalling of a substance known as epidermal growth factor (EGF). Under normal circumstances, EGF may promote blood vessel development, Ganju says.

Previous studies have also found that THC can shrink brain tumours. Nevertheless, experts caution people against smoking marijuana. "I wouldn't advise that. It could make the cancer grow faster," says Ganju, noting that THC might encourage the growth of breast cancer. He adds that that "a lot of work needs to be done" before scientists fully understand how THC affects tumours.

While some studies have found no link between cannabis use and cancer, others have concluded that cannabis smoking is "more harmful" than tobacco because the smoke is inhaled more deeply into the lungs.

Ganju's team presented the new findings this week at the annual meeting of the American Association for Cancer Research in Los Angeles, California, US.

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Cannabis extracts may shrink brain tumours and other cancers by blocking the growth of the blood vessels which feed them, suggests a new study.

An active component of the street drug has previously been shown to improve brain tumours in rats. But now Manuel Guzmán at Complutense University, Spain, and colleagues have demonstrated how the cannabis extracts block a key chemical needed for tumours to sprout blood vessels – a process called angiogenesis.

And for the first time, the team has shown the cannabinoids impede this chemical in people with the most aggressive form of brain cancer - glioblastoma multiforme.

Cristina Blázquez at Complutense University, and one of the team, stresses the results are preliminary. “But it’s a good point to start and continue,” she told New Scientist. “The cannabinoid inhibits the angiogenesis response - if a tumour doesn’t do angiogenesis, it doesn’t grow,” she explains. “So if you can improve angiogenesis on one side and kill the tumour cells on the other side, you can try for a therapy for cancer.”

“This research provides an important new lead compound for anti-cancer drugs targeting cancer’s blood supply,” says Richard Sullivan, head of clinical programmes, at Cancer Research UK.

Fat molecule
The team tested the effects of delta-9-tetrahydrocannabinol in 30 mice. They found the marijuana extract inhibited the expression of several genes related to the production of a chemical called vascular endothelial growth factor (VEGF).

VEGF is critical for angiogenesis, which allows tumours to grow a network of blood vessels to supply their growth. The cannabinoid significantly lowered the activity of VEGF in the mice and two human brain cancer patients, the study showed.

The drug did this by increasing the activity of a fat molecule called ceramide, suggests the study, as adding a ceramide inhibitor stifled the ability of the cannabinoid to block VEGF.

Small and pallid
“We saw that the tumours [in mice] were smaller and a bit pallid,” adds Blázquez. The paleness of the cancer reflected its lack of blood supply as a result of the treatment. In the human patients, she says: “It seems that it works, but it’s very early.”

Sullivan points out: “Although this work is at an early stage of development other research has already demonstrated that VEGF is an important drug target for a range of cancers.”

He emphasises the need for further work on cannabinoid combinations. “Cannabinoids would need to generate very strong data in the future as there are already a number of VEGF inhibitors in clinical development,” he says.

The two patients in the ongoing study are among 14 in a clinical trial of the drug. The patients are given one cycle of treatment, lasting a few days, and their survival and general health are being studied.

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Delta-9-tetrahydrocannabinol enhances breast cancer growth and metastasis by suppression of the antitumor immune response.
In the current study, we tested the central hypothesis that exposure to Delta-9-tetrahydrocannabinol (Delta9-THC), the major psychoactive component in marijuana, can lead to enhanced growth of tumors that express low to undetectable levels of cannabinoid receptors by specifically suppressing the antitumor immune response. We demonstrated that the human breast cancer cell lines MCF-7 and MDA-MB-231 and the mouse mammary carcinoma 4T1 express low to undetectable levels of cannabinoid receptors, CB1 and CB2, and that these cells are resistant to Delta9-THC-induced cytotoxicity. Furthermore, exposure of mice to Delta9-THC led to significantly elevated 4T1 tumor growth and metastasis due to inhibition of the specific antitumor immune response in vivo. The suppression of the antitumor immune response was mediated primarily through CB2 as opposed to CB1. Furthermore, exposure to Delta9-THC led to increased production of IL-4 and IL-10, suggesting that Delta9-THC exposure may specifically suppress the cell-mediated Th1 response by enhancing Th2-associated cytokines. This possibility was further supported by microarray data demonstrating the up-regulation of a number of Th2-related genes and the down-regulation of a number of Th1-related genes following exposure to Delta9-THC. Finally, injection of anti-IL-4 and anti-IL-10 mAbs led to a partial reversal of the Delta9-THC-induced suppression of the immune response to 4T1. Such findings suggest that marijuana exposure either recreationally or medicinally may increase the susceptibility to and/or incidence of breast cancer as well as other cancers that do not express cannabinoid receptors and are resistant to Delta9-THC-induced apoptosis.

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